UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

Wednesday, April 21, 2010

MEMORANDUM

Subject: Acute Toxicity Review for EPA Reg. No.: 5813-RNN
Product Name: ***PUMA***
DP Barcode: D375736

From: Ian Blackwell, Biologist
Chemistry and Toxicology Team
Product Science Branch
Antimicrobials Division (7510P)

Through: Karen Hicks, Team Leader
Chemistry and Toxicology Team
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To: Emily Mitchell, PM 32/ Wanda Henson
Regulatory Management Branch
Antimicrobials Division (7510P)

Applicant: The Clorox Company

FORMULATION FROM LABEL:

Active Ingredient(s):	% by wt.
Sodium hypochlorite	8.25
Other Ingredient(s):	91.75
Total:	100.00

I BACKGROUND: The Clorox Company has submitted an acute inhalation toxicity study, and, cited several other acute toxicity studies to support the registration of their new product, "Puma". Several of these studies were conducted in the 1970s.

The registrant supports four of six acute toxicity study requirements with the following data citations:

Acute Toxicity Studies Cited for EPA File Symbol 5813-RNN	
Study Requirement	MRID Number
Acute Oral Toxicity	00007285
	00007374
	00007274
Acute Dermal Toxicity	00007285
	00007374
	00007277
Primary Eye Irritation	00007374
	00007274
Primary Dermal Irritation	00007374
	00007277
Dermal Sensitization	466723-02

Eurofins | PSL conducted the acute inhalation toxicity study, MRID Number 480175-02. (Eurofins | PSL was formerly known as Product Safety Laboratories, Inc.)

In MRID Number 480175-03, the Clorox Company cites a dermal sensitization study. That study, MRID Number 480175-03, was conducted using Registration Number 5813-52.

II FINDINGS:

1. The Chemistry and Toxicology Team (CTT) searched for each of the cited studies. We found that Industrial BioTest (IBT) conducted several of them. In the 1970's, 1980 and 1990's, the EPA, FDA, and, Health Protection Branch (HPB) of the Canadian Department of Health and Welfare had substantial problems with IBT. The 98th Congress published their Sixty-Third Report by the Committee on Government Operations titled Problems Plague the Environmental Protection Agency's Pesticide Registration Activities in 1984. On page 28, under section A titled FALSIFIED STUDIES SUBMITTED BY INDUSTRIAL BIOTEST LABORATORIES, the committee states:

   "The EPA and HPB validation reviews took approximately 5 years and showed that only about 10 percent of the over 2000 IBT studies which had been submitted in support of pesticide registrations were valid."

Page 30 of that same document reports the Health Effects Division (of the EPA) as saying:

> "We have determined during the review of all the IBT studies that most of the studies were invalid. It seems that every time we turned around, we uncovered another IBT study that somebody didn't know about, and wasn't in the original list, and we made a determination as reflected in the first decision that we not waste our resources validating or attempting to validate any more studies, but to just call them invalid, period, and require replacement, if we stumbled across any more studies that we hadn't previously identified."

2. Also, the New York Times reported in their article E.P.A. THREATENS TO SUSPEND APPROVAL OF PESTICIDES OVER TEST FLAWS on July 12, 1983:

> "The agency told makers of 34 pesticide tested by Industrial Bio-Test, one of the biggest testing laboratories in the country, that they had 90 days to offer new test data or make a commitment to do further work to obtain data. If they failed to do so, registration of the products would be suspended, meaning the pesticides could not be sold legally." "The Industrial Bio-Test case was referred to the Justice Department in 1978."

Testing Facilities of Studies Cited for 5813-RNN/ Puma	
Master Record IDentification (MRID) Number	Conducting Facility
*00007285	Industrial BioTest
*00007374	Industrial BioTest
*00007274	Report cannot be located
*00007277	WARF Institute

* - Please note that these MRIDs report the results of more than one toxicity study.

III RECOMMENDATIONS:

1. The Chemistry and Toxicology Team (CTT) must reject any studies that Industrial BioTest (Bio-Test) conducted.

2. CTT cannot locate MRID Number 00007274. The Clorox Company will have to provide a copy of the report themselves, or, provide other data.

3. The WARF institute study, MRID Number 00007277, is not acceptable. While CTT has not conducted a formal review of this study, it is apparent that this study will not meet FIFRA guidelines. Obvious problems with this study are:

A. As the WARF Institute conducted this study prior to the Agency's 1984 advent of the Good Laboratory Practices (GLP), it has no GLP statement and they could not have conducted the study in accordance with GLPs.
B. The lab dosed the animals at 20 g/kg b.w. According to the Agency's Pesticide Assessment Guidelines, Subdivision F, §III, A, "In the acute dermal toxicity guidelines section, however, the upper dose level is 2 g/kg, rather than the lower limit for Toxicity Category IV, 20 g/kg." This section also states, "... 2 g/kg is a more reasonable approximation of the largest dose which a human could possibly absorb through skin."

4. CTT bridges the dermal sensitization study from Reg. No. 5813-52 to support File Symbol 5813-RNN. The study is recent (2005) and CTT finds the formulas of these two products to be Substantially Similar.

5. The Clorox Company must address the data requirements for the acute oral toxicity, acute dermal toxicity, primary eye irritation and primary skin irritation studies. The registrant has data gaps for these four studies.

The acute toxicity profile for File Symbol 5813-RNN is currently:

Study	MRID Number	Toxicity Category	Study Status
Acute Oral Toxicity	00007285	?	Rejected
	00007374	?	Rejected
	00007274	?	Missing Report/ Data Gap
Acute Dermal Toxicity	00007285	?	Rejected
	00007374	?	Rejected
	00007277	?	Unacceptable
Acute Inhalation Toxicity	480175-02	IV	Acceptable
Primary Eye Irritation	00007274	?	Missing Report/ Data Gap
	00007374	?	Rejected
Primary Skin Irritation	00007374	?	Rejected
	00007277	?	Unacceptable
Dermal Sensitization	466732-02	Nonsensitizer	Cited

IV LABELING:

1. CTT cannot prescribe precautionary labeling for 5813-RNN until the registrant adequately addresses each of the acute toxicity study requirements.

DATA REVIEW FOR ACUTE INHALATION TOXICITY (§81-3, 870.1300)

Product Manager: 32 **Reviewer:** I. Blackwell
MRID No.: 480175-02 **Study Completion Date:** 2/24/2010
Lab Study No.: 28781

Testing Laboratory: Eurofins | PSL
Author: Jennifer Durando, B.S.

Quality Assurance (40 CFR §160.12): Included

Test Material: PUMA Formula No. 2009.0092; "clear, light yellow liquid"
Concentration: gravimetric = 2.18 mg/L ; nominal = 7.36 mg/L

Species: Sprague-Dawley-derived albino rats
Weight: Males= 312-343 g Females= 216-221 g
Age: 9-10 weeks
Source: Ace Animals, Inc.

Summary:

1. **LC_{50} (mg/L)** **Males** > 2.18 mg/L
   Females > 2.18 mg/L
   Combined > 2.18 mg/L
2. **The estimated LC_{50} is** greater than 2.18 mg/L of air.
3. **MMAD:** 2.05 **µm**
4. **Toxicity Category:** IV **Classification:** Acceptable

Procedure (Deviation From §81-3): None

Results:

Reported Mortality

Exposure Concentration	(NUMBER DEATHS/NUMBER TESTED)		
	Males	Females	Combined
2.18 mg/L	0/5	0/5	0/10

Chamber Atmosphere			
Dose Level	MMAD	GSD	particles < 4.7 µm
2.18 mg/L	2.05 µm	1.975 µm	88.3%

Chamber Environment	
Chamber Volume	6.7 liters
Airflow	25.5
Temperature	20-22°C
Relative Humidity	56-60%

Clinical Observations: Facial staining around nose, irregular respiration, dry rales.

Gross Necropsy Findings: No gross abnormalities.